

CLAIMS

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1. An isolated DNA sequence according to Figure 1A and variants and alleles thereof that codes for expression of the human Death Inducer-Obliterator 1 (DIO-1) gene.

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2. A DNA sequence according to claim 1, wherein the DNA sequence is that given in Figure 1A.

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3. An isolated DNA sequence according to Figure 1B and variants and alleles thereof that codes for expression of the murine Death Inducer-Obligator 1 (DIO-1) gene.

4. A DNA sequence according to claim 3, wherein the DNA sequence is that given in Figure 1B.

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5. A fragment of an isolated DNA sequence according to any of claims 1 to 4, which comprises an N-terminal domain, a central non-canonical Zn finger domain, and a C-terminus domain containing a K-rich region.

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6. An isolated DIO-1 polypeptide derived from the DNA sequence according to any of claims 1 to 2 comprising the mature human amino acid sequence shown in Figure 1C and variants thereof.

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7. A polypeptide according to claim 6 comprising the mature human amino acid sequence shown in Figure 1C.

8. An isolated DIO-1 polypeptide derived from the DNA sequence according to any of claims 3 to 4 comprising the mature murine amino acid sequence shown in Figure 1D and variants thereof.

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9. A polypeptide according to claim 8 comprising the mature murine amino acid sequence shown in Figure 1D.

10. A nucleic acid probe for the detection of a nucleic acid sequence encoding a polypeptide according to any of claims 6-9 in a sample.
11. A nucleic acid probe according to claim 10 wherein said probe comprises at least 14 contiguous nucleotides of the sequence given in Figure 1A or 1B.
12. A DNA sequence of any of claims 1 to 5 wherein the isolated DNA comprises a cDNA sequence.
13. An expression vector containing a DNA sequence of any of claims 1-5.
14. A cell transformed with a DNA sequence of any of claims 1-5, such that it allows the direct replication and expression of said DNA sequence.
15. A cell according to claim 14 wherein said cell is a mammalian or a bacterial cell
16. A process for producing a protein according to any of claims 6 to 9 which process comprises the culture of a cell of any of claims 14 to 15 in a suitable culture medium and the isolation of the protein therefrom.
17. A method for identifying clones encoding a DIO-1 polypeptide according to any of claims 6-9, said method comprising screening a genomic or cDNA library with a nucleic acid probe according to any of claims 10 to 11 under low stringency hybridization conditions, and identifying those clones which display a substantial degree of hybridization to said probe.
18. A method of identifying agonists and antagonists of the protein according to any of claims 6-9 comprising transduction or transfection of a mammalian cell line with an expression vector comprising nucleic acid sequences lacking the nuclear localization sequences or lacking the Zn finger domain or lacking the acidic domain or lacking the lysine-rich domain and thereafter identifying the agonist or antagonist interacting with the DIO-1 gene according to claims 6-9.
19. An agonists or antagonists according to claim 18.

20. A method of identifying ligands with which the polypeptide according to any of claims 6-9, interacts, following cloning into and expression in appropriate vectors and using the two-hybrid method.
- 5 21. A method to produce specific monoclonal and polyclonal antibodies against the polypeptide according to any of claims 6 to 9 comprising the injection of the polypeptide to a mammalian.
- 10 22. Method for treatment of diseases which are characterized by the alteration in cell death or by hyperproliferation, characterized by the administration of compounds according to any of claims 6 to 9 or 19.
- 15 23. Method according to claim 22 by administration of a therapeutically effective amount of the compound.
24. Method according to claim 22 in which the disease is cancer, an autoimmune disease and/or diabetes.
- 20 25. Method according to claim 22 in which the disease is rheumatoid arthritis, benign and malignant tumors or hyperproliferative skin disorders.
- 25 26. Method for treatment of diseases which are characterized in the alteration in cell death or by hyperproliferation, comprising introducing into a mammal a nucleic acid vector according to claim 13 and wherein said nucleic acid vector is capable of transforming a cell *in vivo* and expressing said polypeptide in said transformed cell.
- 30 27. A pharmaceutical formulation comprising compounds according to any of claims 6 to 9 or 19 and one or more therapeutically acceptable excipients.
28. A method for identifying a ligand to the compound according to any of claims 6 to 9 or 19, by a cell-based reporter assay, transgenic-animal reporter assay or *in vitro*-binding assay.
- 35 29. A method for identifying a substance for treatment of a condition affected by a polypeptide according to any of claims 6 to 9, comprising screening for an agonist or an antagonist of the polypeptide signal transduction to be used for treating metabolic, proliferative or inflammatory conditions.

~~30.~~ A compound according to any of claims 6 to 9 or 19 for use as a medicament.

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